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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,145	12/05/2001	Liora Cahalon	B12/31	4185
7590 05/05/2004				
C/O THE POLKINGHORNS 9003 FLORIN WAY UPPER MARLBORO, MD 20772			EXAMINER HUI, SAN MING R	
			ART UNIT	PAPER NUMBER
			1617	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/002,145

Applicant(s)

CAHALON ET AL.

Examiner

San-ming Hui

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 5,6,9,13,22,23,26 and 29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,7,8,10-12,14-21,24,25,27,28 and 30-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the specie DS Po912 in response filed February 13, 2004 is acknowledged. The traversal is on the ground(s) that all of the claimed oligosaccharides are sufficiently related according to an inventive concept. This is not found persuasive because the number of species encompassed by the claims are very large. The claims encompass all derivatives of heparin or heparin-sulfate. In the claims, four specific groups of derivatives are recited: N-sulfated-4-deoxy-4-en-iduronoglucosamine, N-sulfated-4-deoxy-4-en-glucuronoglucosamine, N-acetylated-4-deoxy-4-en-glucuronoglucosamine, and N-acetylated-4-deoxy-4-en-iduronoglucosamine. However, the number of the oligosaccharides and the specific structure of these compounds are not specific recited. The specific compounds recited are the ones recited in claims 7, 11, 24, and 27. Therefore, the search for all species encompassed by the claims is diverse and present undue burden to the Office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5, 6, 9, 13, 22, 23, 26, and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in response filed February 13, 2004.

Claims 1-4, 7-8, 10-12, 14-21, 24-25, 27-28, and 30-32 are examined to the extent they read on the elected species.

As the elected species DS Po912 is found free of prior art, the search has extended to other N-sulfated species recited claims 11 and 27. As the N-sulfated species are found free of prior art, the search has extended to other N-sulfated-4-deoxy-4-en-glucuronoglucosamine.

Priority

It is noted that this application appears to claim subject matter disclosed in prior Application No. 09/495,723, filed on February 1, 2000, currently pending, which is a divisional of US Patent Application No. 08/486,127, filed on June 7, 1995 and now issued as US Patent No. 6,020,323, on February 1, 2000, which is a continuation of US Patent Application No. 08/436,330, filed on May 10, 1995, now US Patent No. 5,861,382, issued on January 19, 1999, which claims priority from PCT Application No. PCT/US93/10868, filed on November 9, 1993, and which is a continuation in part of US Patent Application No. 08/096,739, filed on July 3, 1993, abandoned, which is a continuation in part of US Patent Application No. 07/974,750, filed on November 10, 1992, abandoned, which is a continuation in part of US Patent Application No. 07/878,188, tiled on May 1, 1992, abandoned. However, the subject matter of employing the specific heparin or heparin sulfate derivatives recited in claims 11 and 27 to treat cancer by interfering CXCR4 7TM-GPCR signaling pathway are not found to be supported in the applications in which the instant application claims priority from.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 7-8, 10-12, 14-21, 24-25, 27-28, and 30-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment for cancers recited in claim 15 except for colon cancers, does not reasonably provide enablement for other cancers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence of absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art
- 7) the predictability of the art, and
- 8) the breadth of the claims.

Applicant fails to set forth the criteria that define what kind of "maglinancy" would be effectively treated by employing the instant method. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these maglinant disorders without undue experimentation. In the instant case, heparin sulfate is known to enhance the growth of certain types of colon cells (See Timar et al., Invasion Metastasis, 1990;10:301-315, particularly the abstract). Furthermore, only a limited number of "maglinant disorders" examples are set forth, thereby failing to provide sufficient working examples. The instant claims read on all "maglinancy", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 8, 10, 14-21, 25, and 30-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "oligosaccharide is heparin or heparin-sulfate derived" recited in claim 1 renders the claims indefinite as to the compounds encompassed by the claims.

The expression "glucosamine derivative" recited in claims 3 and 19 renders the claims indefinite as to the compounds encompassed by the claims.

Claims 7 and 24 recites the limitation "in which X_1 is hydrogen X_1 and X_2 are sulfates" in lines 3-6. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 8, 10, 14-21, 25, and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over '318 (US patent 4,882,318) in view of Vlodaysky et al. (Adv. Exp. Med. Biol., 992;13:317-327).

'318 teaches heparin and its related molecules for the treatment of tumor by inhibit heparanase activity and thereby decrease the metastasis of the tumor (See the abstract, col. 1 – 2). '318 teaches the dose of heparin and its related molecules useful for treating tumor metastasis as 50-500 μ g/kg/day (See claim 1).

'318 does not expressly teach the herein oligosaccharide compounds for treating tumor metastasis.

Vlodaysky et al. teaches to optimize cancer therapy, one would want to chose a heparin compounds that has low potential for bFGF release but a high inhibition of heparanase activity (See page 317-320). Vlodaysky et al. teaches various factors would affect the heparanase inhibition activity and the bFGF release activity. Those factors are the size, sulfation, acetylation, the position where sulfation or desulfation of the heparin molecules (usually at the N- position) (See page 321-324, particularly, Fig. 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the herein claimed heparin molecules for the treatment of cancer.

One of ordinary skill in the art would have been motivated to employ the herein claimed heparin molecules for the treatment of cancer. From the teachings of the cited prior art, modifying heparin oligosaccharide compounds with different sulfation at the N-


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position to the herein claimed heparin oligosaccharide compounds in order to maximized the heparanase inhibition, which is the mechanism to reduce tumor metastasis, would be reasonably expected to be useful in reducing tumor metastasis and thereby treating cancer.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


San-ming Hui
Patent Examiner
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